UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,866	05/29/2001	Brian Sorrentino	1340-1-021CIP2	4688

31949 7590 07/28/2005

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,866	SORRENTINO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 10, 2005 has been entered.

The Declaration of Dr. Sorrentino, Supplemental Declaration of Dr. Sarkadi, and exhibits submitted on 2/18/05 have been considered. Claims 16, 17, 21-28 are pending in the application and under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed **genus** of invention, for reasons of record and following.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

These claims are drawn to a genus of antibodies that recognize an extracellular portion of a BCRP in its natural conformation. However, neither the sequences nor a consensus chemical structure of the antibodies are disclosed in the specification as filed. As such the claimed invention has not been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention.

In the declaration of Dr. Sorrentino submitted February 2005, the inventor disclosed four antibodies designated as 5D3, 7A3, 1C5, and 8C2, which have been produced (Exhibit A) allegedly according to the method disclosed in the instant application. However, neither the structure-functional relationship of the named antibodies nor how their structures relate to that of the genus of the claimed antibodies are taught. For example, whether these four antibodies (which appear to be found sometime after the priority date) bear structural similarities or have a common

consensus region that relates to their function of recognizing the extracellular portion of the BCRP in its natural conformation, which information may guide future discoveries.

In the response filed February 2005, applicants argue "the antibodies produced had the same well-characterized structure of any other conventional antibody" and "using this art-accepted characterization of an antibody, applicants believe they have met the requirement under 35 USC 112, first paragraph".

In response, the claimed antibody is not just any antibody, but a genus of antibodies with a specific function. Although the general structure of an antibody is well known in the art, the identifying characteristics of the genus should be the structure that determines the binding specificity of the antibody, i.e. not bind to any BCRP antigen in any conformation, but bind to the extracellular portion in its natural conformation. Such structure was not known at the time of the instant filing, and thus, it is applicant's duty to disclose such. Applicants are reminded that the rejection was made in view of the state of the art that no prior art of record discloses such an antibody, and because of the unpredictability in the art as indicated in the declarations of a skilled artisan, Dr. Sarkadi. Therefore, except for the four named antibodies, the instant disclosure does not provide an adequate written description of the claimed genus in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the invention as it is broadly claimed.

Applicant is referred to the Revised Interim Guidelines for "Written Description" requirement published December 21, 1999 in the Federal Register, Volume 64, Number 244, pages 71427-71440. "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY

DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436). The skilled artisan cannot envision the detailed chemical structure of the genus encompassed by the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the genus of antibodies. Therefore, only the described 5D3, 7A3, 1C5, and 8C2 meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using anti-BCRP antibodies 5D3, 7A3, 1C5, and 8C2, does not reasonably provide enablement for making and using the claimed genus of anti-BCRP antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for reasons of record and following.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

In the instant case, while the disclosed method of making the antibody and the need for producing an antibody recognizing the extracellular portion of a ABC transporter protein in a natural conformation were known in the art as taught by *Mechetner et al* (US 5,994,088), the state of the art was illustrated in the declaration and supplemental declaration of Dr. Sarkadi, who has repeatedly indicated that as of the instant priority date, "*there was **no reliable** method known in the art for producing an isolated antibody that recognizes an extracelluar portion of the ABC transporter BCRP in a living cell. The production of antibodies to any ABC transporter can only be*

evaluated on a case-by-case basis". Dr. Sarkadi's supplemental declaration also indicated "*while it would be reasonable to try the various methods known in the art, the reasonable expectation of successfully producing an antibody that recognizes the extracelluar portion of BCRP in its natural conformation could not be anticipated*". Thus, considering the state of the art, and the statement of Dr. Sarkadi's declarations, it is unpredictable to reliably produce the claimed antibody, and it would require undue experimentation to search for the genus of antibodies that meet claim limitation.

Although Dr. Sorrentino has recently disclosed four antibodies designated as 5D3, 7A3, 1C5, and 8C2, which belong to the family (genus) of the antibodies that recognize an extracellular portion of the BCRP in its natural conformation, the structures of the antibodies or a consensus structure of the genus have not been taught. For reasons set forth on record and stated in the declaration and supplemental declaration of Dr. Sarkadi, it is highly unpredictable whether the antibodies having the function required by the claims could be reproducibly made without undue experimentation.

In order to enable the claimed invention, the antibodies must be readily available or obtainable by a repeatable method set forth in the specification or other wise known and readily available to the public. If it is not so obtainable or available, an enabling deposit of the antibodies may satisfy the requirements of 35 U.S.C. 112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance

by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Claims 21 and 25 are drawn to a polyclonal antibody, however it appears only monoclonal antibodies are disclosed in the declaration of Dr. Sorrentino. Claims 23, 24, 27, and 28 are drawn to chimeric and humanized antibodies, however, since the disclosed antibodies are not readily available to the public, since no sequence information of the disclosed antibodies are available in the specification or subsequent disclosure, it would have require undue experimentation for the skilled intending to practice the invention to make the claimed chimeric and humanized antibodies. Thus, the disclosure fails to support the full scope of the claimed invention.

Accordingly, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, 17, 21-28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Ross et al* (US 6,313,277, IDS/AA), in view of *Mechetner et al* (US 5,994,088), for reasons of record and following.

It is noted that applicants' arguments to different sections of the rejections and in different declarations contradict themselves. On one hand, applicants state, "*The amino acid sequence and characterization of BCRP as an ABC transporter was well-established in the art at the time of filing of the instant application*" (page 6, 2nd paragraph, 2/05 Remarks), and continued to state "Applicants clearly provide at page 39 of the instant application the detailed steps which can be, and were carried out to overexpress a known BCRP nucleotide sequence in a living cell to produce an antibody to a naturally conformed extracellular portion of BCRP", and "Applicants appreciated the necessity of producing BCRP in its natural conformation in living cells" (page 6, 3rd paragraph). To this end, applicants are reminded that the amino acid sequence and characterization of BCRP as an ABC transporter and necessity of generating an anti-BCRP antibody were taught by *Ross et al*; the method of making and the necessity of producing an antibody that recognizes an ABC transporter in its natural conformation in a living cell was taught by *Mechetner et al*. Thus, following these teachings, and according to the logic of the arguments, the skilled artisan would have had a reasonable expectation of success producing an antibody that recognizes extracellular portion of a BCRP in its natural conformation.

In the February 2005 response, Applicant submitted a declaration by Dr. Sorrentino, who stated, "*Having definitely generated more than one antibody that recognizes an extracellular portion of BCRP in its natural conformation on living cells, this method is clearly a validated method for generating an antibody to an extracellular portion of this particular ABC transporter in its natural conformation. I expect that the robustness of this method will allow for routine generation of additional antibodies of the type claimed by simply repeating the procedures disclosed in the '586 and '866 applications*" (emphasis added).

When considering the declarations along with the disclosure of the specification and the state of the art as a whole,. It is noted the genus of the claimed antibody could be reasonably produced by the combined the teachings of *Ross et al* and *Mechetner et al*, and which rendered the claimed invention obvious. The statement of Dr. Sorrentino supports the conclusion of the instant rejection, i.e. following the combined teachings and routine experimentation, one would have had a reasonable expectation of success in generating antibodies of the type. Accordingly, the rejection stands.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
July 22, 2005